

**AMENDMENTS TO THE SPECIFICATION:**

Pursuant to the revised 37 § CFR 1.121, please amend the specification as follows:

On the title page, please replace the title "Cytokine Polypeptides and Nucleic Acids" with the following title: "Cytokine Polypeptides".

On page 1, line 1, please replace the title "Cytokine Polypeptides and Nucleic Acids" with the following title: "Cytokine Polypeptides".

Please replace the paragraph beginning at page 1, line 28 with the following amended paragraph:

It is desirable to modify the relative populations of T<sub>H</sub>1 and T<sub>H</sub>2 cells in various circumstances. Modulators which up-regulate T<sub>H</sub>1-mediated responses by, for example, directing the differentiation of naive T cells into T<sub>H</sub>1 cells, inducing T<sub>H</sub>1 cell proliferation, and increasing IFN- $\gamma$  production and macrophage activation, are useful in promoting cell-mediated immunity to infectious agents such as bacterial, protozoan, intracellular parasitic and viral infections. Modulators which down-regulate T<sub>H</sub>1-mediated responses are useful in situations where a decreased cell-mediated immune response is ~~in~~ desired, for example, in treatment of autoimmune diseases such as multiple sclerosis.

Please replace the paragraph beginning at page 2, line 17 with the following amended paragraph:

In one aspect, the invention includes an isolated or recombinant nucleic acid encoding a modified cytokine polypeptide of the invention. Included are polynucleotide sequences comprising a mature polypeptide coding region of a sequence selected from SEQ ID NO:1 to SEQ ID NO:7, or SEQ ID NO:16 to SEQ ID NO:25 ~~SEQ ID NO:35~~, and

complementary polynucleotide sequences thereof. Polynucleotide sequences encoding a polypeptide comprising a mature polypeptide region of an amino acid sequence selected from SEQ ID NO:8 to SEQ ID NO:14 or SEQ ID NO:26 to SEQ ID NO:35, and complementary polynucleotide sequences thereof, are also a feature of the invention. Similarly, a polynucleotide sequence which hybridizes under at least highly stringent conditions over substantially the entire length of any one of the preceding polynucleotide sequences is a feature of the invention. A polynucleotide sequence which encodes a polypeptide comprising an amino acid sequence having at least about 90% sequence identity to a mature polypeptide region of a sequence selected from SEQ ID NO:8 to SEQ ID NO:14 and SEQ ID NO:39, or to a mature polypeptide region of a sequence selected from SEQ ID NO:26 to SEQ ID NO:35 and SEQ ID NO:40, is also a feature of the invention. In various embodiments, the polynucleotide sequence encodes a polypeptide comprising an amino acid sequence having at least about 90%, 92%, 95%, 96%, 97%, 98%, or 99% identical to a mature polypeptide region of a sequence selected from SEQ ID NO:8 to SEQ ID NO:14 and SEQ ID NO:39, or to a mature polypeptide region of a sequence selected from SEQ ID NO:26 to SEQ ID NO:35 and SEQ ID NO:40. In addition, a polynucleotide sequence comprising a nucleotide fragment of any of the preceding polynucleotide sequences, which nucleotide fragment encodes a polypeptide having T-cell proliferative activity and/or IFN-gamma induction activity in T-cells (*e.g.*, human T-cells) in the presence of a p35 polypeptide or a p40 polypeptide is also a feature of the invention.

Please replace the paragraph beginning at page 12, line 28 with the following amended paragraph in which a period is added at the end of the paragraph:

The invention also includes a polypeptide which specifically binds polyclonal antisera raised against at least one antigen, the at least one antigen comprising a polypeptide sequence selected from an amino acid sequence set forth in SEQ ID NO:8 to SEQ ID NO:14 or SEQ ID NO:26 to SEQ ID NO:35 or a fragment thereof. In particular, the invention provides polypeptides which bind a polyclonal antisera raised against at least one antigen, wherein said at

least one antigen comprises at least one amino acid sequence set forth in SEQ ID NO:8 to SEQ ID NO:14, or a fragment of any of these amino sequences, wherein the polyclonal antisera is subtracted with one or more known p40 polypeptides or proteins, including, *e.g.*, a polypeptide or protein encoded by a nucleic acid having or corresponding to one or more of the following GenBank<sup>TM</sup> accession numbers: M65272 and M65290 (human), U19841 (*Macaca mulatta*, rhesus monkey), U19834 (*Cercocebus torquatus*, sooty mangabey), Y11129 (*Equus caballus*, horse), U83184, Y07762 and AF054607 (*Felis catus*, cat), U49100 and AF091134 (*Canis familiaris*, dog), U57752 and U10160 (*Cervus elaphus*, red deer), AF007576 (*Capra hircus*, goat), AF004024 (*Ovis aries*, sheep), U11815 (*Bos taurus*, cow), U08317 (*Sus scrofa*, pig), X97019 and AF082494 (*Marmota monax*, woodchuck), AF133197 and U16674 (*Rattus norvegicus*, rat), M86671 and S82426 (*Mus musculus*, mouse), AF097507 (*Cavia porcellus*, guinea pig), and AF046211 (*Mesocricetus auratus*, golden hamster), and other similar or homologous p40 nucleic acid sequences presented in, *e.g.*, GenBank.

Please replace the paragraph beginning at page 13, line 16 with the following amended paragraph:

The invention also provides polypeptides which bind a polyclonal antisera raised against at least one antigen, wherein said at least one antigen comprises at least one amino acid sequence set forth in SEQ ID NO:26 to SEQ ID NO:35, or a fragment of any of these amino sequences, wherein the polyclonal antisera is subtracted with one or more known p35 polypeptides or proteins, including, *e.g.*, a polypeptide or protein encoded by a nucleic acid having or corresponding to one or more of the following GenBank accession numbers:[::] M65271, M65291 (human); U19842 (*Macaca mulatta*, rhesus monkey), U19835 (*Cercocebus torquatus*, sooty mangabey), U83185, Y07761, AF054605 (*Felis catus*, cat), U49085 (*Canis familiaris*, dog), L35765 (*Sus scrofa*, pig), Y11130 (*Equus caballus*, horse), U14416 (*Bos taurus*, cow), U57751 (*Cervus elaphus*, red deer), AF173557 (*Ovis aries*, sheep), AF003542 (*Capra hircus*, goat), X97018 (*Marmota monax*, woodchuck), AF177031 (*Rattus norvegicus*, rat), and

M86672, S82419 (*Mus musculus*, mouse), and other similar or homologous p35 nucleic acid sequences presented in, *e.g.*, GenBank.

Please replace the paragraph beginning at page 12, line 10 with the following amended paragraph:

The invention also includes compositions produced by digesting one or more nucleic acid described above with, *e.g.*, a restriction endonuclease, an RNase, or a DNase; compositions produced by fragmenting one or more nucleic acid described above by mechanically shearing, by UV, or by chemical methods; and compositions produced by incubating one or more nucleic acid described above in the presence of ribonucleotide or deoxyribonucleotide ~~deoxyribonucleotide~~ triphosphates and a nucleic acid polymerase, *e.g.*, a thermostable polymerase.

Please replace the paragraph beginning at page 16, line 10 with the following amended paragraph:

In general, nucleic acids and proteins derived by mutation of the sequences herein are a feature of the invention. Similarly, those produced by diversity generation methods or recursive sequence recombination ("RSR") methods (*e.g.*, DNA shuffling) are a feature of the invention. Mutation and recombination methods using the nucleic acids described herein are a feature of the invention. For example, one method of the invention includes recursively recombining one or more nucleic acid sequences of the invention as described above and below with one or more additional nucleic acids (including, but not limited to, those noted herein), each sequence of the one or more additional nucleic acids encoding a modified p40 polypeptide or modified p35 polypeptide or an amino acid subsequence thereof. The recombining steps are optionally performed *in vivo*, *ex vivo*, *in silico* or *in vitro*. Said diversity generation or recursive sequence recombination produces at least one library of recombinant modified p40 or modified p35 nucleic acids. Also included in the invention are a recombinant modified p40 nucleic acid produced by this method, a recombinant modified p35 nucleic acid produced by this method, a

cell containing the recombinant modified p40 nucleic acid or recombinant modified p35 nucleic acid, a nucleic acid library produced by recursive sequence recombination or other diversity generation methods, a composition comprising two or more of recombinant modified p40 or modified p35 nucleic acids, and a population of cells comprising such recombinant modified p40 or modified p35 nucleic acids or containing the library. In one embodiment, the library comprises ~~comprise~~ at least ten such recombinant nucleic acids.

Please replace the paragraph beginning at page 46, line 29 with the following amended paragraph:

In addition, essentially any nucleic acid can be custom ordered from any of a variety of commercial sources, such as The Midland Certified Reagent Company (mcrc@oligos.com), The Great American Gene Company (see website at genco.com) (~~http://www.genco.com~~), ExpressGen Inc. (see website at expressgen.com) (~~www.expressgen.com~~), Operon Technologies Inc. (Alameda, CA) and many others. Similarly, peptides and antibodies can be custom ordered from any of a variety of sources, such as PeptidoGenic (pkim@ccnet.com), HTI Bio-products, Inc. ~~inc.~~ (see website at htbio.com.) ~~http://www.htbio.com~~), BMA Biomedicals Ltd. (U.K.), Bio.Synthesis, Inc., and many others.

Please replace the paragraph beginning at page 62, line 8 with the following amended paragraph:

In addition to expression of the nucleic acids of the invention as gene replacement nucleic acids, the nucleic acids are also useful for sense and anti-sense suppression of expression, *e.g.*, to down-regulate expression of a nucleic acid of the invention, once expression of the nucleic acid is no-longer desired in the cell. Similarly, the nucleic acids of the invention, or subsequences or anti-sense sequences thereof, can also be used to block expression of naturally occurring homologous nucleic acids. A variety of sense and anti-sense technologies are known in the art, *e.g.*, as set forth in Lichtenstein and Nellen (1997) *Antisense Technology: A Practical*

*Approach* IRL Press at Oxford University, Oxford, England, and in Agrawal (1996) *Antisense Therapeutics* ~~Therapeutics~~ Humana Press, NJ, and the references cited therein.

Please replace the paragraph beginning at page 16, line 10 with the following amended paragraph:

$$T_m (^{\circ}\text{C}) = 79.8^{\circ}\text{C} + 18.5 (\log_{10}M) + 0.58 (\%G + C) - 11.8(\%G + C)^2 - 0.56 (\%f) - \frac{820}{n}$$
~~where  $\frac{820}{n}$ , where~~ M is the molarity of the monovalent cations (usually Na<sup>+</sup>), (%G + C) is the percentage of guanosine (G) and cystosine (C) nucleotides, (%f) is the percentage of formamide and n is the number of nucleotide bases (*i.e.*, length) of the hybrid. *Id.*

Please replace the paragraph beginning at page 102, line 18 with the following amended paragraph:

In other embodiments, the invention provides a modified p35 polypeptide comprising an amino acid sequence having at least about 90% amino acid sequence identity to the sequence identified herein as the mature polypeptide region (amino acid residue positions 23-219) of SEQ ID NO:40: R-X<sub>24</sub>-LP-X<sub>27</sub>-X<sub>28</sub>-T-X<sub>30</sub>-X<sub>31</sub>-PG-X<sub>34</sub>-X<sub>35</sub>-X<sub>36</sub>-CL-X<sub>39</sub>-X<sub>40</sub>-SQNLL-X<sub>46</sub>-A-X<sub>48</sub>-SN-X<sub>51</sub>-LQ-X<sub>54</sub>-A-X<sub>56</sub>-Q-X<sub>58</sub>-LEFY-X<sub>63</sub>-CTSEE-X<sub>69</sub>-DHEDIT-X<sub>76</sub>-DKTSTVEACLPLEL-X<sub>91</sub>-X<sub>92</sub>-NESCL-X<sub>98</sub>-SR-X<sub>101</sub>-X<sub>102</sub>-S-X<sub>104</sub>-ITNGSCLASRKTSFM-X<sub>120</sub>-X<sub>121</sub>-LC-X<sub>124</sub>-X<sub>125</sub>-SIYEDLKMYQ-X<sub>136</sub>-EFK-X<sub>140</sub>-MNAKLLM-X<sub>148</sub>-PKRQIFLDQNML-X<sub>161</sub>-X<sub>162</sub>-I-X<sub>164</sub>-EL-X<sub>167</sub>-QALN-X<sub>172</sub>-NSET-X<sub>177</sub>-PQK-X<sub>181</sub>-SLEE-X<sub>186</sub>-DFYKTKIKLCILLHAFRIRAVTI-X<sub>210</sub>-R-X<sub>212</sub>-X<sub>213</sub>-SYLN-X<sub>218</sub>-S, or a conservatively substituted variation thereof, where X<sub>24</sub> is N or S; X<sub>27</sub> is V or T; X<sub>28</sub> is A or T; X<sub>30</sub> is P or A; X<sub>31</sub> is D, S, or G; X<sub>34</sub> is M or R; X<sub>35</sub> is F, S, or L; X<sub>36</sub> is P or is deleted; X<sub>39</sub> is H or D; X<sub>40</sub> is H or Y; X<sub>46</sub> is R or K; X<sub>48</sub> is V or A; X<sub>51</sub> is M or T; X<sub>54</sub> is K or R; X<sub>56</sub> is K or R; X<sub>58</sub> is T or I; X<sub>63</sub> is P or S; X<sub>69</sub> is I or T; X<sub>76</sub> is K or Q; X<sub>91</sub> is A or I; X<sub>92</sub> is K or T; X<sub>98</sub> is N or A; X<sub>101</sub> is E or G; X<sub>102</sub> is T or I; X<sub>104</sub> is F or L; X<sub>120</sub> is T; X<sub>121</sub> is T; X<sub>124</sub> is L or H; X<sub>125</sub> is S or G; X<sub>136</sub> is V or M; X<sub>140</sub> is T or A; X<sub>148</sub> is D or N; X<sub>161</sub> is A or T; X<sub>162</sub> is V or A; X<sub>164</sub> is D or A; X<sub>167</sub> is M or L; X<sub>172</sub> is F or V; X<sub>177</sub> is V or A; X<sub>181</sub> is S or P; X<sub>186</sub> is P or L; X<sub>210</sub> is D or N; X<sub>212</sub> is M; X<sub>213</sub> is M; and X<sub>218</sub> is S.

In various embodiments, the modified p35 polypeptide comprises an amino acid sequence having at least about 90% ~~about 90%~~, 92%, %, 95%, 96%, 97%, 98%, or 99% amino acid sequence identity to the mature polypeptide region (amino acid residue positions 23-219) of SEQ ID NO:40. The invention also includes a polynucleotide sequence encoding said polypeptide or a fragment of said polypeptide having proliferative activity in a human T-cell based assay or interferon-gamma induction activity in a human T-cell based assay.

Please replace the paragraph beginning at page 106, line 21 with the following amended paragraph:

Another preferred example of algorithm that is suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul *et al.*, 1977, *Nuc. Acids Res.* 25: 3389-3402 and Altschul *et al.*, 1990, *J. Mol. Biol.* 215: 403-410, respectively. BLAST and BLAST 2.0 are used with the parameters described herein to determine percent sequence identity for the nucleic acids and proteins of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (see website at [ncbi.nlm.nih.gov](http://ncbi.nlm.nih.gov)) (~~[www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)~~). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al.*, *supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation

of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, M=5, N=-4 and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (*see* Henikoff & Henikoff (1989) *Proc. Nat'l Acad. Sci. U.S.A.* 89: 10915) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a comparison of both strands.

Please replace the paragraph beginning at page 109, line 26 with the following amended paragraph:

In another embodiment, a mature modified p40 polypeptide of the present invention comprises the following sequence (amino acid residue positions 23-238 of SEQ ID NO:39): IWEL-X<sub>27</sub>-K-X<sub>29</sub>-VYVVELDWYP-X<sub>40</sub>-APGE-X<sub>45</sub>-VVL-X<sub>49</sub>-CDTPEEDGITWT-X<sub>62</sub>-DQSS-X<sub>67</sub>-VLG-X<sub>71</sub>-GKTLTI-X<sub>78</sub>-VKEFGDAGQYTC-X<sub>91</sub>-KGG-X<sub>95</sub>-X<sub>96</sub>-LS-X<sub>99</sub>-SLLLLHKKEDGIWSTDILKDQK-X<sub>122</sub>-PK-X<sub>125</sub>-K-X<sub>127</sub>-FL-X<sub>130</sub>-CEAK-X<sub>135</sub>-YSG-X<sub>139</sub>-FTCWWLT-X<sub>147</sub>-ISTDL-X<sub>153</sub>-F-X<sub>155</sub>-VKSSRGS-X<sub>163</sub>-DP-X<sub>166</sub>-GVTCG-X<sub>172</sub>-X<sub>173</sub>-X<sub>174</sub>-LS-X<sub>177</sub>-X<sub>178</sub>-X<sub>179</sub>-X<sub>180</sub>-X<sub>181</sub>-X<sub>182</sub>-X<sub>183</sub>-X<sub>184</sub>-X<sub>185</sub>-X<sub>186</sub>-X<sub>187</sub>-X<sub>188</sub>-Y-X<sub>190</sub>-VECQE-X<sub>196</sub>-SACP-X<sub>201</sub>-AEESLPIEV-X<sub>211</sub>-X<sub>212</sub>-X<sub>213</sub>-A-X<sub>215</sub>-HKLKYENYTS-X<sub>226</sub>-FFIRDIKPDPPKNLQL-X<sub>244</sub>-PLKNSR-X<sub>251</sub>-VE-X<sub>254</sub>-X<sub>255</sub>-W-X<sub>257</sub>-YPDTWS-X<sub>264</sub>-PHSYFSLTF-X<sub>274</sub>-X<sub>275</sub>-QVQG-X<sub>280</sub>-X<sub>281</sub>-KRE-X<sub>285</sub>-X<sub>286</sub>-X<sub>287</sub>-X<sub>288</sub>-X<sub>289</sub>-F-X<sub>291</sub>-D-X<sub>293</sub>-TSA-X<sub>297</sub>-V-X<sub>299</sub>-C-X<sub>301</sub>-K-X<sub>303</sub>-A-X<sub>305</sub>-I-X<sub>307</sub>-V-X<sub>309</sub>-A-X<sub>311</sub>-DRY-X<sub>315</sub>-SS-X<sub>318</sub>-WS-X<sub>321</sub>-WASV-X<sub>326</sub>-X<sub>327</sub>-X<sub>328</sub>, or a conservatively substituted variation thereof,

where X<sub>27</sub> is K or E; X<sub>29</sub> is D or N; X<sub>40</sub> is D or N; X<sub>45</sub> is M or T; X<sub>49</sub> is T or A; X<sub>62</sub> is S; X<sub>67</sub> is E or G; X<sub>71</sub> is T; X<sub>78</sub> is H; X<sub>91</sub> is H or R; X<sub>95</sub> is E, A, K, or T; X<sub>96</sub> is V or A; X<sub>99</sub> is R or Q; X<sub>122</sub> is E or K; X<sub>125</sub> is N or A; X<sub>127</sub> is S or I; X<sub>130</sub> is K; X<sub>135</sub> is N or D; X<sub>139</sub> is R or H; X<sub>147</sub> is T or A; X<sub>153</sub> is T or K; X<sub>155</sub> is S or T; X<sub>163</sub> is S or T; X<sub>166</sub> is Q, R, or H; X<sub>172</sub> is A or T; X<sub>173</sub> is A or V; X<sub>174</sub> is T or L; X<sub>177</sub> is A or E; X<sub>178</sub> is E or D; X<sub>179</sub> is R, L, or K; X<sub>180</sub> is V or G; X<sub>181</sub> to X<sub>184</sub>



inclusive is deleted or is replaced with the sequence S-(L or M)-(E or D)-H-R; X<sub>185</sub> is E; X<sub>186</sub> is Y; X<sub>187</sub> is K or N; X<sub>188</sub> is K; X<sub>190</sub> is R or T; X<sub>196</sub> is G; X<sub>201</sub> is A or S; X<sub>211</sub> is V; X<sub>212</sub> is V or L; X<sub>213</sub> is D or E; X<sub>215</sub> is V or I; X<sub>226</sub> is S or R; X<sub>244</sub> is K or R; X<sub>251</sub> is Q or H; X<sub>254</sub> is V or I; X<sub>255</sub> is S or N; X<sub>257</sub> is E or G; X<sub>264</sub> is T or A; X<sub>274</sub> is C or G; X<sub>275</sub> is V or I; X<sub>280</sub> is K or R; X<sub>281</sub> is S or N; X<sub>285</sub> is K or D; X<sub>286</sub> is K or R; X<sub>287</sub> is D or is deleted; X<sub>288</sub> is R or is deleted; X<sub>289</sub> is I or L; X<sub>291</sub> is T or M; X<sub>293</sub> is K or Q; X<sub>297</sub> is T or K; X<sub>299</sub> is I, T, or V; X<sub>301</sub> is R or H; X<sub>303</sub> is N or D; X<sub>305</sub> is K; X<sub>307</sub> is R; X<sub>309</sub> is Q; X<sub>311</sub> is R; X<sub>315</sub> is Y or H; X<sub>318</sub> is S or F; X<sub>321</sub> is E or D; X<sub>326</sub> is P or S; X<sub>327</sub> is C or L; and X<sub>328</sub> is S, G, or Q. As defined above, a conservatively modified variation of the above sequence can include up to a total of about 15 amino acid deletions, insertions, or conservative substitutions in the 306 amino acid sequence, excluding the positions designated X, which correspond to the amino acid explicitly defined. The polypeptide may further comprise an N-terminal leader sequence M-X<sub>2</sub>-X<sub>3</sub>-QQLV-X<sub>8</sub>-SWFSLV-X<sub>15</sub>-LASPL-X<sub>21</sub>-A (amino acid residue positions 1-22 of SEQ ID NO:39), or a conservatively modified variation thereof, where X<sub>2</sub> is C or H; X<sub>3</sub> is H or P; X<sub>8</sub> is I or V; X<sub>15</sub> is F or L; and X<sub>21</sub> is V or M.

Please replace the paragraph beginning at page 110, line 26 with the following amended paragraph:

In another embodiment, a mature modified p35 polypeptide of the present invention comprises the following sequence (amino acid residue positions 23-219 of SEQ ID NO:40): R-X<sub>24</sub>-LP-X<sub>27</sub>-X<sub>28</sub>-T-X<sub>30</sub>-X<sub>31</sub>-PG-X<sub>34</sub>-X<sub>35</sub>-X<sub>36</sub>-CL-X<sub>39</sub>-X<sub>40</sub>-SQNLL-X<sub>46</sub>-A-X<sub>48</sub>-SN-X<sub>51</sub>-LQ-X<sub>54</sub>-A-X<sub>56</sub>-Q-X<sub>58</sub>-LEFY-X<sub>63</sub>-CTSEE-X<sub>69</sub>-DHEDIT-X<sub>76</sub>-DKTSTVEACLPLEL-X<sub>91</sub>-X<sub>92</sub>-NESCL-X<sub>98</sub>-SR-X<sub>101</sub>-X<sub>102</sub>-S-X<sub>104</sub>-ITNGSCLASRKTSFM-X<sub>120</sub>-X<sub>121</sub>-LC-X<sub>124</sub>-X<sub>125</sub>-SIYEDLKMYQ-X<sub>136</sub>-EFK-X<sub>140</sub>-MNAKLLM-X<sub>148</sub>-PKRQIFLDQNML-X<sub>161</sub>-X<sub>162</sub>-I-X<sub>164</sub>-EL-X<sub>167</sub>-QALN-X<sub>172</sub>-NSET-X<sub>177</sub>-PQK-X<sub>181</sub>-SLEE-X<sub>186</sub>-DFYKTKIKLCILLHAFRIRAVTI-X<sub>210</sub>-R-X<sub>212</sub>-X<sub>213</sub>-SYLN-X<sub>218</sub>-S, or a conservatively substituted variation thereof,

where X<sub>24</sub> is Nor S; X<sub>27</sub> is V or T; X<sub>28</sub> is A or T; X<sub>30</sub> is P or A; X<sub>31</sub> is D, S, or G; X<sub>34</sub> is M or R; X<sub>35</sub> is F, S, or L; X<sub>36</sub> is P or is deleted; X<sub>39</sub> is H or D; X<sub>40</sub> is H or Y; X<sub>46</sub> is R or K; X<sub>48</sub> is V or A; X<sub>51</sub> is M or T; X<sub>54</sub> is K or R; X<sub>56</sub> is K or R; X<sub>58</sub> is T or I; X<sub>63</sub> is P or S; X<sub>69</sub> is I or T;

X<sub>76</sub> is K or Q; X<sub>91</sub> is A or I; X<sub>92</sub> is K or T; X<sub>98</sub> is N or A; X<sub>101</sub> is E or G; X<sub>102</sub> is T or I; X<sub>104</sub> is F or L; X<sub>120</sub> is T; X<sub>121</sub> is T; X<sub>124</sub> is L or H; X<sub>125</sub> is S or G; X<sub>136</sub> is V or M; X<sub>140</sub> is T or A; X<sub>148</sub> is D or N; X<sub>161</sub> is A or T; X<sub>162</sub> is V or A; X<sub>164</sub> is D or A; X<sub>167</sub> is M or L; X<sub>172</sub> is F or V; X<sub>177</sub> is V or A; X<sub>181</sub> is S or P; X<sub>186</sub> is P or L; X<sub>210</sub> is D or N; X<sub>212</sub> is M; X<sub>213</sub> is M; and X<sub>218</sub> is S. As defined above, a conservatively modified variation of the above sequence can include up to a total of about 10 amino acid deletions, insertions, or conservative substitutions in the 219 amino acid sequence, excluding the positions designated X, which correspond to the amino acid explicitly defined. The polypeptide may further comprise the N-terminal leader sequence M-X<sub>2</sub>-P-X<sub>4</sub>-R-X<sub>6</sub>-LLL-X<sub>10</sub>-X<sub>11</sub>-TLVLL-X<sub>17</sub>-HLVL-X<sub>22</sub> (amino acid residue positions 1-22 of SEQ ID NO:40), or a conservatively modified variation thereof, where X<sub>2</sub> is C or Y; X<sub>4</sub> is A, L or P; X<sub>6</sub> is S or G; X<sub>10</sub> is V or I; X<sub>11</sub> is A or S; X<sub>17</sub> is D or H; and X<sub>22</sub> is A or G.

Please replace the paragraph beginning at page 115, line 18 with the following amended paragraph:

In one typical format, the immunoassay uses a polyclonal antiserum which was raised against one or more polypeptide comprising sequences corresponding to one or more of : SEQ ID NO:8 to SEQ ID NO:14 and SEQ ID NO:26 to SEQ ID NO:35, or a substantial subsequence thereof (*i.e.*, at least about 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 98% of the full length sequence provided). The full set of potential polypeptide immunogens derived from SEQ ID NO:8 to SEQ ID NO:14 and SEQ ID NO:26 to SEQ ID NO:35 are collectively referred to below as "the immunogenic polypeptides." The resulting antisera is optionally selected to have low cross-reactivity against the control p40 polypeptides or the control p35 polypeptides, and/or other known p40 or p35 polypeptides, and any such cross-reactivity is removed by immunoabsorption ~~immunoabsorbition~~ with one or more of the control p40 or p35 polypeptides and/or other known p40 or p35 polypeptides, prior to use of the polyclonal antiserum in the immunoassay.

Please replace the paragraph beginning at page 117, line 29 with the following amended paragraph:

As a final determination of specificity, the pooled antisera is optionally fully immunoabsorbed ~~immunosorbed~~ with the *immunogenic* polypeptide(s) (rather than the control polypeptides) until little or no binding of the resulting immunogenic polypeptide subtracted pooled antisera to the immunogenic polypeptide(s) used in the immunoabsorption ~~immunosorption~~ is detectable. This fully immunoabsorbed ~~immunosorbed~~ antisera is then tested for reactivity with the test polypeptide. If little or no reactivity is observed (i.e., no more than 2x the signal to noise ratio observed for binding of the fully immunoabsorbed ~~immunosorbed~~ antisera to the immunogenic polypeptide), then the test polypeptide is specifically bound by the antisera elicited by the immunogenic polypeptide.

Please replace the paragraph beginning at page 136, line 24 with the following amended paragraph:

The assay was performed as described by Punnonen and de Vries (1994; *Journal of Immunology* 152: 1094). Human peripheral blood leukocytes (PBLs) were isolated from buffy coats by density-gradient centrifugation using Histopaque (Sigma), washed twice with PBS, and resuspended at a concentration of  $2 \times 10^6$  cells/ml in RPMI medium (Gibco-BRL) supplemented with 10% fetal calf serum (Hyclone), 1X glutamine (Gibco-BRL) and 100 ug/ml ~~100ug/ml~~ of penicillin and streptomycin (Gibco-BRL). The isolated PBLs were then cultured in T75 flasks for 96 hours in the presence of 5 ug/ml ~~5ug/ml~~ phytohemagglutinin (PHA; Sigma) to induce activation of T-lymphocytes. Subsequently, the cells were washed twice with PBS and adjusted to  $4 \times 10^5$  cells/ml in RPMI medium.

Please replace the paragraph beginning at page 137, line 3 with the following amended paragraph:

Assays were performed either (a) directly on serial dilutions of culture supernatants from transfected mammalian cells, or (b) on proteins purified from culture

supernatants. Serial dilutions of expression culture medium, or of partially purified protein, were placed in 96-well round bottom plates (Costar). A 100 microliter (ul) aliquot of resuspended T-cells, activated as described above, was immediately added to each well with an automated multi-channel pipet (Matrix) and the plates were incubated at 37°C with 5% CO<sub>2</sub> for 48 hours. This was followed by an additional incubation period of 16 hours in the presence of 1 uCi ~~1 uCi~~ of <sup>3</sup>H-thymidine (Amersham). The cells were then harvested and the amount of <sup>3</sup>H-thymidine incorporation – a measure of cytokine-dependent T<sub>H</sub>1 proliferation - was measured using a 1450 micro-beta Trilux liquid scintillation counter (Wallac).

Please replace the paragraph beginning at page 137, line 14 with the following amended paragraph:

Production of a human T<sub>H</sub>1 specific cytokine, interferon-γ, was measured using a modification of the method described by Murphy *et al.* (1985; *Journal of Experimental Medicine* 164:263). Human T-cells were purified by negative selection using antibodies to CD14, CD19, CD56 and CD16 (Beckton-Dickinson). The homogenous population of T-cells was cultured at 1x10<sup>6</sup> cells/well for 5 days in Iscove medium, in the presence or absence of test proteins. Before activating the cells with soluble anti-CD3 (5 ug/ml) (~~5ug/ml~~) and anti-CD28 (5 ug/ml) (~~5ug/ml~~), the cells were harvested and washed with PBS. The cells were incubated at 37°C with 5% CO<sub>2</sub> for 48 hours prior to harvesting the conditioned medium and measuring the level of interferon-γ with a commercially available ELISA kit (R&D Systems).